

SUBSTITUTE SEQUENCE LISTING

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<120> HUMANIZED ANTIBODIES AGAINST CD3

<130> 05882-0176-CNUS03

<140> US 09/618,380

<141> 2000-07-18

<150> US 08/397,411

<151> 1995-03-01

<150> US 07/859,583

<151> 1992-03-27

<160> 14

<170> PatentIn version 3.1

<210> 1

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain of Humanized 1D10 Ab minus signal sequence

<400> 1

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val 35 40 45

Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 85 90 95

Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 2

<211> 107

<212> PRT

<213> Mus sp.

<400> 2

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val

35 40 45

Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Thr Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Lys Gln Phe Ser Leu Lys Ile Asn Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Gly Asn Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 85 90 95

Pro Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 3

<211> 116

<212> PRT

<213> Artificial Sequence

<220>

<223> Heavy chain of Humanized 1D10 Ab minus signal sequence

<400> 3

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val

Thr Val Ser Ser 115

<210> 4

<211> 116

<212> PRT

<213> Mus sp.

<400> 4

Gln Val Gln Leu Lys Gln Ser Gly Pro Gly Leu Val Gln Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Gly Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Y J

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Phe 65 70 75 80

Lys Met Asn Ser Leu Gln Ala Asp Asp Thr Ala Met Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val

Thr Val Ser Ser 115

<210> 5

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Complete light chain of Humanized 1D10 Ab

<400> 5

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Asn Ile Tyr Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Val 35 40 45

Ser Asn Ala Lys Thr Leu Ala Glu Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Lys Gln Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His His Tyr Gly Asn Ser Tyr 85 90 95

Pro Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 155 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175 Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205

Phe Asn Arg Gly Glu Cys 210

<210> 6

<211> 273

<212> PRT

<213> Artificial Sequence

<220>

<223> Fd-jun in F(ab'-zipper)2 of humanized 1D10 antibody

<400> 6

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu 180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 210 215 220

Cys Pro Pro Cys Lys Cys Pro Ala Gly Gly Arg Ile Ala Arg Leu Glu 225 230 235 240

Glu Lys Val Lys Thr Leu Lys Ala Gln Asn Ser Glu Leu Ala Ser Thr 245 250 255

Ala Asn Met Leu Arg Glu Gln Val Ala Gln Leu Lys Gln Lys Val Met 260 265 270

Asn

<210> 7

<211> 446

<212> PRT

<213> Artificial Sequence

<220>

<223> Complete heavy chain of Humanized 1D10 Ab

<400> 7

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Lys Trp Ser Gly Gly Ser Thr Glu Tyr Asn Ala Ala Phe Ile 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 70 75 80

Lys Leu Asn Ser Leu Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Asn Asp Arg Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
100 105 110

Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala 115 120 125

Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu 130 135 140

Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
145 150 155 160

Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser 165 170 175

Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Leu 180 185 190

Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr 195 200 205

Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr 210 215 220

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly · 370 375. Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

<210> 8

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Light chain of Humanized M291 Ab minus signal sequence

<400> 8

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 9

<211> 106

<212> PRT

<213> Mus sp.

<400> 9

Asp Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Lys Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Thr Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr 85 90 95

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 10

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Heavy chain of Humanized M291 Ab minus signal sequence

<400> 10

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Ser Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr His Tyr Asn Gln Lys Leu

50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Ala Tyr Tyr Asp Tyr Asp Gly Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 11

<211> 120

<212> PRT

<213> Mus sp.

<400> 11

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Ser Tyr 20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr His Tyr Asn Gln Lys Leu 50 55 60

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Ala Tyr Tyr Asp Tyr Asp Gly Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ala 115 120

<210> 12

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Complete light chain of Humanized M291 Ab

<400> 12

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Arg Leu Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Pro Thr 85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro 100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr 115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys 130 135 140 Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu 145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser 165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala 180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe 195 200 205

Asn Arg Gly Glu Cys 210

<210> 13

<211> 279

<212> PRT

<213> Artificial Sequence

<220>

<223> Complete heavy chain of Humanized M291 Ab

<400> 13

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Ser Tyr 20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met 35 40 45

Gly Tyr Ile Asn Pro Arg Ser Gly Tyr Thr His Tyr Asn Gln Lys Leu 50 55 60

Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ala Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser Ala Tyr Tyr Asp Tyr Asp Gly Phe Ala Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val 165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Lys Cys Pro Ala Gly Gly Leu Thr 225 230 235 240

Asp Thr Leu Gln Ala Glu Thr Asp Gln Leu Glu Asp Lys Lys Ser Ala 245 250 255

Leu Gln Thr Glu Ile Ala Asn Leu Leu Lys Gly Lys Glu Lys Leu Glu 260 265 270

Phe Ile Leu Ala Ala Thr Ser 275

<210> 14

<211> 7

- <212> PRT
- <213> Artificial Sequence
- <220>
- <223> Leucine zipper motif
- <220>
- <221> MISC_FEATURE
- <222> (2)..(7)
- <223> Xaa is any amino acid
- <400> 14

Leu Xaa Xaa Xaa Xaa Xaa 1